Preplanned Studies

Weekly Weight Gain in Women with Gestational Diabetes Mellitus and Neonatal Birth Weight — China, 2011–2021

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Summary

What is already known about this topic?

Elevated gestational weight gain (GWG) during pregnancy among women diagnosed with gestational diabetes mellitus (GDM) is correlated with an increased instance of large for gestational age (LGA) and macrosomia. However, it remains uncertain whether managing weekly GWG following a GDM diagnosis positively impacts fetal birth weight.

What is added by this report?

Our study found that GWG following GDM diagnosis correlates positively with the risk of LGA and macrosomia among all body mass index (BMI) subgroups, especially for overweight and obese women.

What are the implications for public health practice?

The results of this research highlight the importance of enforcing a more stringent regulation on GWG on a weekly basis for overweight and obese women diagnosed with GDM, particularly when considering neonatal growth.

Neonatal weight serves as a crucial marker of intrauterine development and maternal nutritional health (*1*). Given the potential cumulative impacts of excessive gestational weight gain (GWG) and gestational diabetes mellitus (GDM) on neonatal weight, it may be beneficial to adopt a slower GWG rate (*2*). However, the benefits of maintaining control over weekly GWG following a GDM diagnosis in relation to fetal birth weight remain undetermined. Consequently, we utilized data from various centers nationwide to evaluate the relationship between weekly GWG post-GDM diagnosis (categorized by weight at GDM diagnosis) and the likelihood of large for gestational age (LGA) and macrosomia. Associations between weekly GWG after GDM diagnosis and risks of LGA and macrosomia were assessed using the odds ratio (*OR*) and 95% confidence interval (*CI*).

Based on the Chinese standards for sex- and gestational age-specific birth weight from 2015 (*3*), LGA is identified as a birth weight higher than the 90th percentile for gestational age defined by sex. Macrosomia is identified as a birth weight exceeding 4,000 g (*4*). Body mass index (BMI) at the time of GDM diagnosis was grouped into nine categories using the statistical equidistant grouping method (*5*): BMI>19 kg/m^2; 19 kg/m$^2 \leq$BMI<21 kg/m^2; 21 kg/m$^2 \leq$BMI<23 kg/m^2; 23 kg/m$^2 \leq$BMI<25 kg/m^2; 25 kg/m$^2 \leq$BMI<27 kg/m^2; 27 kg/m$^2 \leq$BMI<29 kg/m^2; 29 kg/m$^2 \leq$BMI<31 kg/m^2; 31 kg/m$^2 \leq$BMI<33 kg/m^2; and BMI$\geq$33 kg/m^2. The prevalences of LGA and macrosomia were subsequently calculated for each interval. Utilizing univariate and multivariate logistic regression analyses, we explored the association between weight at GDM diagnosis, weekly GWG post-GDM diagnosis, and the risk factors for LGA and macrosomia. All statistical analyses were performed using SAS statistical software (version 9.4, SAS Institute Inc., Cary, NC, USA), with two-sided statistical tests. A *P* value of less than 0.05 was deemed statistically significant.

This retrospective study relied on data collected from seven regional tertiary hospitals in various provincial level administrative divisions (PLADs) throughout China, including Beijing, Shaanxi, Guizhou, Hebei, Zhejiang, and Shandong. These establishments included Peking Union Medical College Hospital, Beijing Tongzhou District Maternal and Child Health Hospital, Dong E County People's Hospital, Northwest Women and Children's Hospital, the Fourth Affiliated Hospital of Hebei Medical University, Guiyang Maternal and Child Health Hospital, and Wenzhou People's Hospital. All selected facilities had established consistent clinical treatment standards for GDM and were known for the reliability of their data. Female GDM patients' records from 2011 to 2021 were analyzed for this project. All information was extracted from electronic medical records, details of which have been discussed in a previous study (*6*). Subjects' weights, usually not

assessed during the 75-g oral glucose tolerance test (OGTT), were documented a week before or after the activity to obtain more comprehensive data. Ultimately, 11,168 women with GDM were considered for this analysis.

Essential data were collected from medical records, which included maternal age, weight prior to pregnancy, week of GDM diagnosis, weight at time of GDM diagnosis, weight before delivery, weeks remaining until delivery, and neonatal birth weight. The diagnostic criteria for GDM are the same as in previous study (6).

Study participants self-reported their pre-pregnancy weight. Using these self-reported measurements, pre-pregnancy BMI was calculated using the formula weight (kg) divided by the square of height (m^2). The pre-pregnancy BMI classification criteria remained the same as in previous study. The pregnant women's weight reported a week before or after undergoing the OGTT was marked as the weight at GDM diagnosis. The corresponding BMI was determined by dividing this weight by the square of height (m^2). Pre-delivery weight refers to the measurements taken one week prior to childbirth. The GWG post-GDM diagnosis was computed by deducting the pre-delivery weight from the weight at GDM diagnosis. Lastly, the rate of GWG after the GDM diagnosis, measured in kg/week, represented the GWG from GDM diagnosis to delivery.

Continuous variables are presented as the mean ± standard deviations. Categorical variables are expressed as frequency (percentage) in the descriptive analysis. We used the univariable and multivariable logistic regression models to estimate the effects of weekly GWG and GWG after GDM diagnosis on the occurrence of LGA and macrosomia. BMI of GDM diagnosis was grouped by equidistant grouping method.

The Peking Union Medical College Hospital (PUMCH) Ethics Committee approved this study (NO. JS-2333). Due to the observational nature of the research and the absence of personally identifiable information collection, informed consent was waived, as previously noted elsewhere (7). The study, registered under ClinicalTrials.gov Identifier: NCT04421053, adhered to the principles laid out in the Declaration of Helsinki.

Table 1 presents the clinical characteristics of the study participants. Our final analysis included 11,168 women diagnosed with GDM. The mean maternal age was 31.02 years with a standard deviation of 4.38. Of these women, 1,338 (11.98%) delivered infants classified as LGA, while 764 (6.84%) delivered infants with macrosomia. Noteworthy variations were observed in the baseline characteristics of women with GDM within the LGA and macrosomia groups.

A statistically significant increase in the *OR* for fetal growth was observed in individuals grouped by normal weight [LGA: adjusted odds ratio (*aOR*)=2.641, 95% *CI*: 1.926–3.622 and macrosomia: *aOR*=3.299, 95% *CI*: 2.217–4.909]. Notably, increased *OR* was also apparent in the overweight (LGA: *aOR*=2.575, 95% *CI*: 1.734–3.823 and macrosomia: *aOR*=1.998, 95% *CI*: 1.223–3.263) and obese groups (LGA: *aOR*=1.056, 95% *CI*: 1.032–1.082). According to pre-pregnancy BMI, more substantial weekly GWG was associated with a higher risk of LGA and macrosomia. Nonetheless, the *OR* for macrosomia in the obese group was not significant (*aOR*=1.741, 95% *CI*: 0.750–4.043). In addition to this, the *OR* for fetal growth increased significantly in the underweight (LGA: *aOR*=1.140, 95% *CI*: 1.083–1.200 and macrosomia: *aOR*=1.165, 95% *CI*: 1.096–1.239), normal weight (LGA: *aOR*=1.096, 95% *CI*: 1.083–1.110 and macrosomia: *aOR*=1.102, 95% *CI*: 1.086–1.120), overweight (LGA: *aOR*=1.096, 95% *CI*: 1.078–1.114 and macrosomia: *aOR*=1.115, 95% *CI*: 1.093–1.138) and obese groups (LGA: *aOR*=1.056, 95% *CI*: 1.032–1.082 and macrosomia: *aOR*=1.050, 95% *CI*: 1.019–1.082) (Table 2). There was a direct correlation observed between weight at the time of GDM diagnosis and the risk of developing LGA and macrosomia.

The data suggests that with an increase in BMI at the point of GDM diagnosis from less than 19 kg/m^2 to equal to or greater than 33 kg/m^2, the incidence of LGA increased markedly from 1.33% to 24.71%. Simultaneously, the prevalence of macrosomia also rose from 1.33% to 15.21%, as indicated in Figure 1.

Further analysis was conducted on the association between BMI at the time of GDM diagnosis and fetal birth weight. Notable findings indicated that an increased *OR* for LGA (*OR*=1.726, 95% *CI*: 1.431–2.083) was observed when the BMI at GDM diagnosis ranged from 23–25 kg/m^2. The odds ratio for LGA also increased in the subsequent four groups after the reference group, showcasing ratios of *OR*=2.169, 95% *CI*: 1.788–2.631, *OR*=3.003, 95% *CI*: 2.440–3.696, *OR*=4.047, 95% *CI*: 3.161–5.181, and *OR*=3.937, 95% *CI*: 2.860–5.420, respectively.

TABLE 1. Clinical characteristics of study participants.

Characteristic	Overall (11,168) (mean±SD)/N (%)	Macrosomia			LGA		
		No (9,207) (mean±SD)/N (%)	Yes (1,338) (mean±SD)/N (%)	P value	No (10,087) (mean±SD)/N (%)	Yes (764) (mean±SD)/N (%)	P value
Age	31.02±4.38	31.02±4.39	31.08±4.38	0.012*	31.03±4.38	30.59±4.26	0.776
Pre-weight (kg)	58.91±8.91	58.48±8.67	63.20±9.21	<0.001†	58.61±8.80	63.08±9.11	<0.001†
Pre-BMI (kg/m²)	22.70±3.17	22.57±3.12	23.88±3.21	<0.001†	22.61±3.15	23.73±3.15	<0.001†
Underweight (<18.5 kg/m²)	810 (7.25)	696 (6.23)	44 (0.39)		770 (6.89)	26 (0.23)	
Normal weight (18.5 kg/m²≤BMI<23.9 kg/m²)	6,835 (61.20)	5,763 (51.60)	689 (6.17)	<0.001†	6,326 (56.64)	403 (3.61)	<0.001
Overweight (24.0 kg/m²≤BMI<27.9 kg/m²)	2,775 (24.85)	2,187 (19.58)	447 (4.00)		2,441 (21.86)	254 (2.27)	
Obese (≥28.0 kg/m²)	748 (6.70)	561 (5.02)	158 (1.41)		640 (5.73)	81 (0.73)	
Diagnostic week	26.20±1.20	26.20±1.20	26.23±1.18	0.048*	26.21±1.20	26.31±1.16	0.236
Weight at the time of GDM diagnosis (kg)	67.27±9.27	66.71±8.95	72.89±9.27	<0.001†	66.84±9.10	73.31±9.36	<0.001†
BMI at the time of GDM diagnosis (kg/m²)	25.92±3.28	25.75±3.21	27.55±3.23	<0.001†	25.79±3.25	27.59±3.26	<0.001†
Weight gain after diagnosis of GDM (kg)	4.81±3.20	4.73±3.20	5.45±3.18	<0.001†	4.78±3.18	5.81±3.14	<0.001†
Weekly GWG after the diagnosis of GDM (kg/week)	0.40±0.26	0.39±0.26	0.45±0.25	<0.001†	0.39±0.26	0.46±0.24	<0.001†
Pre-delivery weight (kg)	72.08±9.67	71.44±9.28	78.34±9.66	<0.001†	71.62±9.44	79.12±9.67	<0.001†
Delivery gestational age (weeks)	38.66±1.44	38.68±1.44	38.64±1.30	<0.001†	38.73±1.28	39.19±0.96	0.019*
Total GWG (kg)	13.17±5.20	12.97±5.11	15.15±5.43	<0.001†	13.01±5.09	16.04±5.50	<0.001†
Neonatal weight (g)	3,340±470	3,290±370	4,010±370	<0.001†	3,310±360	4,230±210	<0.001†

Note: The data is expressed as either the mean ± standard deviation or as a number (%). The independent t-test was utilized to analyze the difference between the two groups' continuous variables, whereas the Chi-square test was employed to compare the categorical data.

Abbreviation: SD=standard deviation; N=number; LGA=large gestational age; BMI=body mass index; GWG=gestational weight gain; GDM=gestational diabetes mellitus.

* P<0.05.
† P<0.001.

TABLE 2. Association between weekly GWG after GDM diagnosis and LGA and macrosomia, stratified by pre-pregnancy BMI status.

Group	Variable	Univariate analysis LGA OR (95% CI)	Macrosomia OR (95% CI)	Multivariate analysis LGA OR (95% CI)	Macrosomia OR (95% CI)
Overall group	Weekly GWG (kg/week)	2.404 (1.931–2.991)†	2.800 (2.120–3.697)†	2.692 (2.148–3.373)†	2.820 (2.125–3.742)†
	Weight at GDM diagnosis (kg)	1.072 (1.065–1.078)	1.072 (1.064–1.080)	1.073 (1.060–1.080)	1.072 (1.064–1.080)
Underweight (<18.5 kg/m²)	Weekly GWG (kg/week)	2.583 (0.755–8.835)	5.414 (1.242–23.593)*	3.022 (0.815–11.197)	6.482 (1.288–32.623)*
	Weight at GDM diagnosis (kg)	1.141 (1.084–1.201)†	1.165 (1.097–1.238)†	1.140 (1.083–1.200)†	1.165 (1.096–1.239)†
Normal weight (18.5 kg/m²≤BMI<23.9 kg/m²)	Weekly GWG (kg/week)	2.615 (1.928–3.548)†	3.598 (2.449–5.285)†	2.641 (1.926–3.622)†	3.299 (2.217–4.909)†
	Weight at GDM diagnosis (kg)	1.096 (1.083–1.110)†	1.104 (1.087–1.121)†	1.096 (1.083–1.110)†	1.102 (1.086–1.120)†
Overweight (24.0 kg/m²≤BMI<27.9 kg/m²)	Weekly GWG (kg/week)	2.932 (2.004–4.290)†	2.653 (1.655–4.253)†	2.575 (1.734–3.823)†	1.998 (1.223–3.263)†
	Weight at GDM diagnosis (kg)	1.097 (1.080–1.115)†	1.119 (1.097–1.142)†	1.096 (1.078–1.114)†	1.115 (1.093–1.138)†
Obese (≥28.0 kg/m²)	Weekly GWG (kg/week)	2.389 (1.275–4.478)*	1.819 (0.799–4.145)	1.056 (1.032–1.082)*	1.741 (0.750–4.043)
	Weight at GDM diagnosis (kg)	1.057 (1.032–1.082)†	1.050 (1.019–1.082)*	1.056 (1.032–1.082)†	1.050 (1.019–1.082)*

Note: Multivariable analysis was performed by adjusting for maternal age and weight gain at the time of GDM diagnosis or weekly GWG.
Abbreviation: GWG=gestational weight gain; GDM=gestational diabetes mellitus; LGA=large gestational age; BMI=body mass index; OR=odds ratio; CI=confidence interval.
* $P<0.05$.
† $P<0.001$.

Contrastingly, a decrease in the odds ratio for LGA was documented when the BMI at GDM diagnosis ranged from 19–21 kg/m^2 or 21–23 kg/m^2, with respective ratios of OR=0.497, 95% CI: 0.310–0.798 and OR=0.588, 95% CI: 0.446–0.777 (Figure 2A). A parallel trend was apparent in the odds ratio for macrosomia (Figure 2B). The findings thus indicate that the risk of LGA occurrence and macrosomia increases with a higher BMI at GDM diagnosis. These findings are also consistent with the results delineated in Table 2.

In the course of our research, we conducted further analyses to investigate the correlation between the weekly GWG post GDM diagnosis and the associative risks of both LGA and macrosomia. As per representation in Figure 2A, a BMI at GDM diagnosis ranging between 19 and 21 kg/m^2 resulted in a significantly high odds ratio of LGA and macrosomia [(OR=1.192, 95% CI: 1.071–1.327), (aOR=1.182, 95% CI: 1.044–1.338)], respectively. Similarly, a BMI range between 23 and 33 kg/m^2 at GDM diagnosis markedly escalated the odds ratio of LGA and macrosomia.

DISCUSSION

Our research suggests that GWG following GDM diagnosis correlates positively with the risk of LGA and macrosomia among all BMI subgroups. Moreover, our findings indicate that the risks of LGA and macrosomia heighten in correspondence to an increase in BMI at the time of GDM diagnosis. These findings underscore the importance of a more stringent oversight of weekly GWG in managing neonatal growth, specifically in women diagnosed with GDM who are classified as overweight or obese.

Women diagnosed with GDM can significantly reduce the risk of macrosomia and LGA by managing their weight. The diagnosis of GDM typically occurs around 24 to 28 weeks of gestation, leaving a relatively short time between diagnosis and delivery. This indicates that GWG rate post-diagnosis may provide a more accurate representation of GWG throughout a GDM pregnancy. One U.S. study reported that a weekly GWG of 1 pound post-diagnosis, adjusted for pre-pregnancy BMI, elevated the risk of adverse outcomes, such as LGA and macrosomia, by approximately 36% to 83% (8).

Our study agreed with these findings, showing a clear correlation between weekly GWG post-diagnosis and the risk of LGA and macrosomia. Further, we
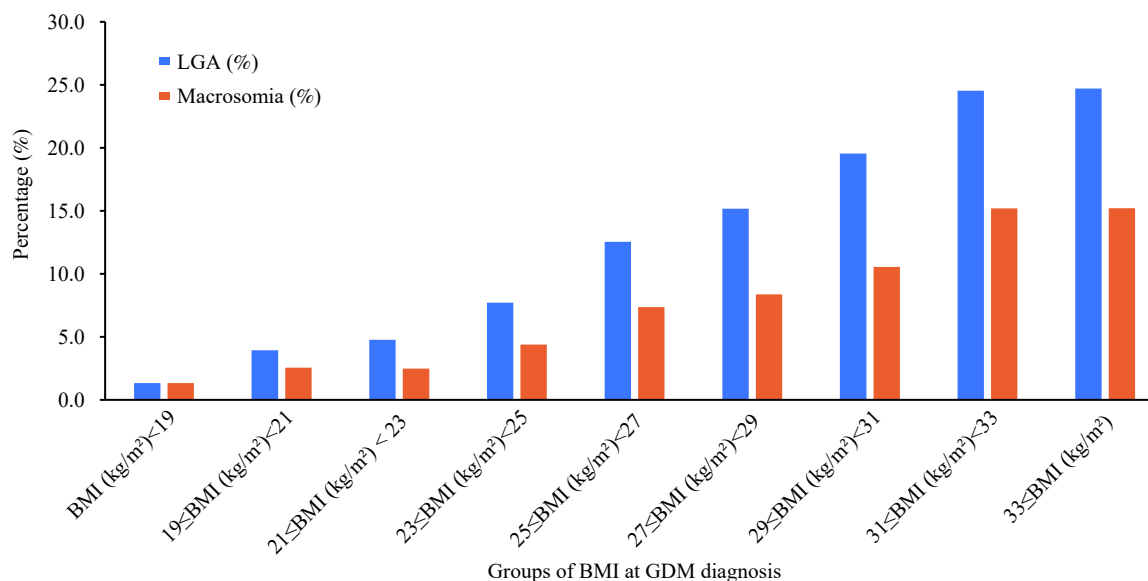
FIGURE 1. Percentage of LGA and macrosomia occurrence in groups stratified by BMI at the time of GDM diagnosis. Abbreviation: LGA=large for gestational age; BMI=body mass index; GDM=gestational diabetes mellitus.

explored this association in relation to BMI at the time of GDM diagnosis.

Barnes et al. (9) performed a retrospective cohort study on pregnant women with excessive GWG prior to GDM diagnosis. They segmented post-diagnosis weight gain into 2-kg units and found a proportional increase in LGA incidence with increased weight gain among GDM patients. This correlates with our findings, but they also examined the impact of excessive weekly GWG post-diagnosis on insulin therapy requirements, an aspect our study did not explore.

In conclusion, clinicians should monitor weekly GWG post-GDM diagnosis closely. It's imperative to conduct interventional studies to understand factors contributing to appropriate GWG, such as diet (10), and develop comprehensive weight management guidelines for women with GDM.

Our study stratified participants into nine subgroups aligned with their BMI at GDM diagnosis, to accommodate the cumulative effects of metabolic status and GWG (11). A subsequent analysis of the correlation between weight at GDM diagnosis and fetal birth weight revealed a direct correlation.

Clinical vigilance is necessary for overweight and obese pregnant women. These women often exhibit varying degrees of pre-pregnancy insulin resistance and/or chronic inflammation. Pregnancy may only serve as a metabolic stress test. Physiological insulin resistance during gestation can exacerbate pre-existing metabolic abnormalities, resulting in pronounced

metabolic shifts in overweight and obese women (12). Excessive glucose is converted into stored body fat, giving rise to macrosomia.

More research is needed to delve into the association between weekly GWG and neonatal growth patterns while mitigating the influence of pre-GDM weight gain.

The present study possesses distinct strengths. Primarily, the sample size selected is robust. Analysis was performed on the data collected from seven hospitals spread across various regions in China, thus providing a comprehensive representation of GWG among GDM affected women in the country. Second, our research probed the correlation between weekly GWG post GDM diagnosis and neonatal birth weight, an aspect not extensively explored by prior studies, which mostly focused on overall GWG. Third, we segmented the study participants into nine groups based on their BMI computed at the time of GDM diagnosis. The subgroup analysis, taking into account weight gain prior to GDM diagnosis, enhances the reliability of our findings.

Nevertheless, this study is not without limitations. Markedly, the primary treatment for GDM is lifestyle adjustment, however, dietary records were not included in the analysis, which may affect the results. Furthermore, certain social determinants such as education level or smoking habits were not available, potentially acting as confounding factors. Lastly, as this is a retrospective cohort study, recall bias could pose a challenge. Hence, it is recommended that future
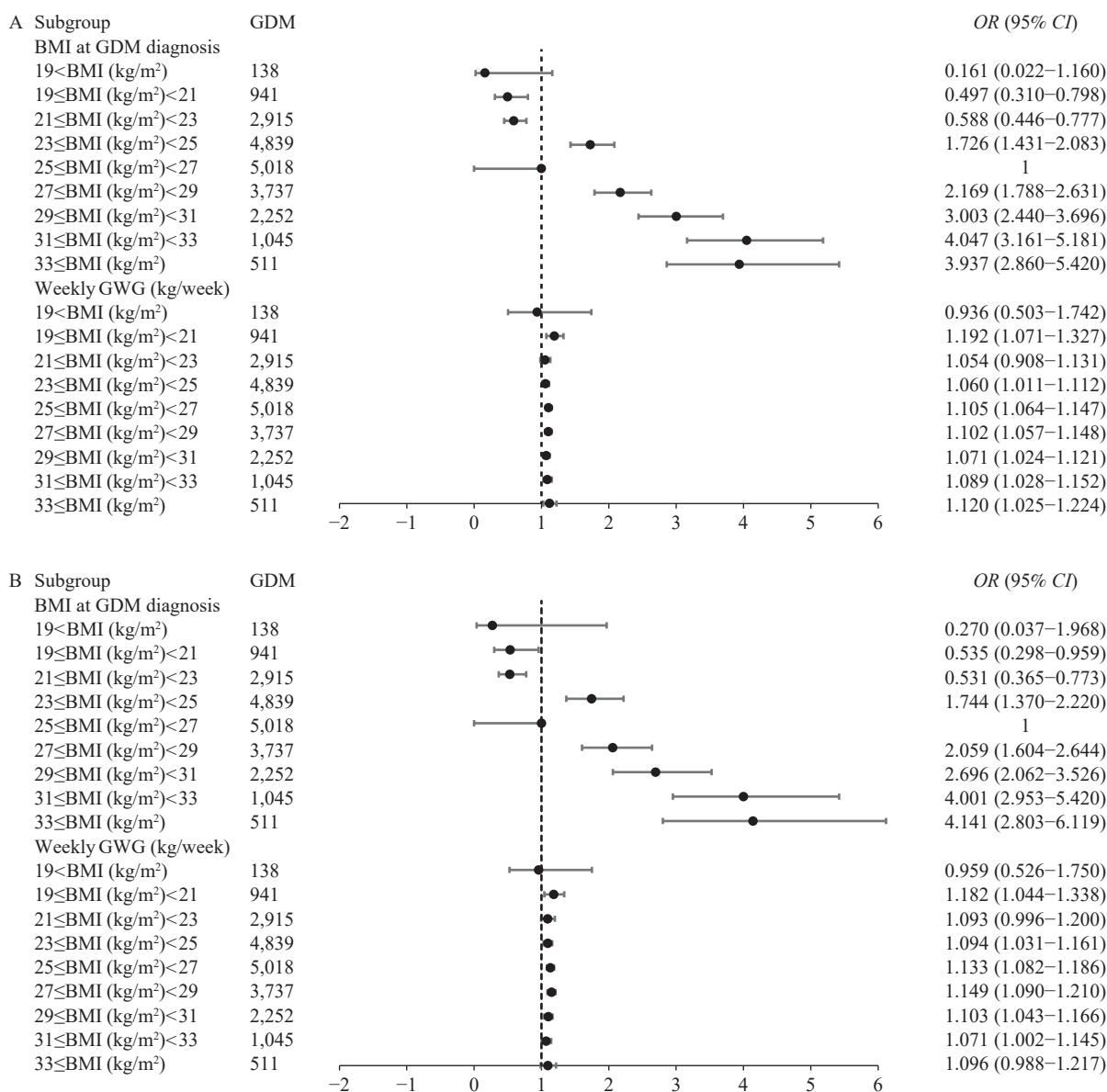
FIGURE 2. Association between various BMI groups at the time of GDM diagnosis, post-diagnosis gestational weight gain, and the risks of LGA and macrosomia.
Abbreviation: GDM=gestational diabetes mellitus; BMI=body mass index; GWG=gestational weight gain; *OR*=odds ratio; *CI*=confidence interval.

prospective cohort studies consider these factors while assessing the connection between weight gain after GDM diagnosis and neonatal birth weight.

In summary, the findings from our data imply a positive correlation between excessive weight gain following GDM diagnosis and increased risks for LGA and macrosomia, particularly in overweight and obese women with GDM. Tighter guidelines for weight gain rate may confer safety and benefits for the population with gestational diabetes.

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